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Changes in the composition of carnitines in hemodialysis patients

To the Editor: In their recent article, Evans et al [1] demonstrated the temporal changes in the level and composition of carnitines before and after the commencement of hemodialysis (HD) in their patients. The author reported the percentage of plasma non-acetyl acyl carnitine increases with a longer duration of HD. The reason for the change in composition, however, is less discussed. We would like to put forward some explanations. Three major enzymes play roles in the transportation of carnitine in mitochondria: carnitine palmitoyltransferase I (CPT-I), carnitine/acylcarnitine translocase (CAT), and carnitine palmitoyltransferase II (CPT-II). The fatty acid is activated as acyl-CoA by acyl-CoA synthetase at the outer mitochondria membrane. Acyl-CoA is then converted to acylcarnitine by the CPT-I between the outer and inner mitochondira membranes. Acylcarnitine, next, is transported across the mitochondrial inner membrane by a CAT. In mitochodria, acylcarnitine acts as a substrate for CPT-II, transferring the acyl group to CoA and releasing carnitine. Acyl CoA then enters the fatty acid β-oxidation pathway [2]. If the activity of CAT or CPT-II decreases, the acylcarnitine will then accumulate and its plasma level will increase. Recent studies [3] have demonstrated marked increase in the ratio of acyl to L-carnitine in primary carnitine disorders (CAT or CPT-II deficiency). Besides, Soejima et al [4] has reported a case of partial CPT deficiency presenting with a higher acyl-to-free carnitine ratio.

The recently discovered organic cation transporter (OCTN2) plays a role in the reabsorption of carnitine and short-chain acyl carnitine in kidneys [5]. This novel transporter may decrease its preference for free carnitine in patients before dialysis. Thus, we suggested the increase in the ratio of acyl/free carnitine in HD patients may possibly result from loss of the preferential excretion of acyl-carnitine by OCTN2, as well as decrease in the activity of CAT or CPT-I.

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Reply from the Authors

We would like to thank the authors for their comments regarding our recently published paper [1]. While we recognize that alterations in the enzymatic activity of CAT, CPT, and OCTN2 may account, at least in part, for the accumulation of acylcarnitines in chronic hemodialysis patients, recent research by our group has suggested an alternative cause for the changes in carnitine pool composition in this population.

A number of studies have investigated the impact of a single hemodialysis session on acylcarnitine levels in hemodialysis patients [2, 3]. These studies demonstrated a significantly higher acylcarnitine to L-carnitine ratio in postdialysis plasma samples compared to predialysis levels, indicating a larger loss of L-carnitine than acylcarnitines into the dialysate.

A recent study by our group investigated the impact of a dialysis session on individual endogenous acylcarnitine levels in chronic hemodialysis patients [4]. The study examined pre- and postdialysis plasma concentrations of L-carnitine and 31 individual acylcarnitines in 50 patients. We demonstrated that 29 out of the 31 acylcarnitines were significantly elevated in the ESRD population when compared to healthy controls. For carnitine esters with an acyl-chain length less than 8 carbons, plasma acylcarnitine levels decreased significantly over the course of the dialysis session; however, levels invariably remained higher than those observed in the healthy population. Once acylcarnitine carbon-chain length exceeded 8 carbons, the dialytic removal of these compounds diminished, with a

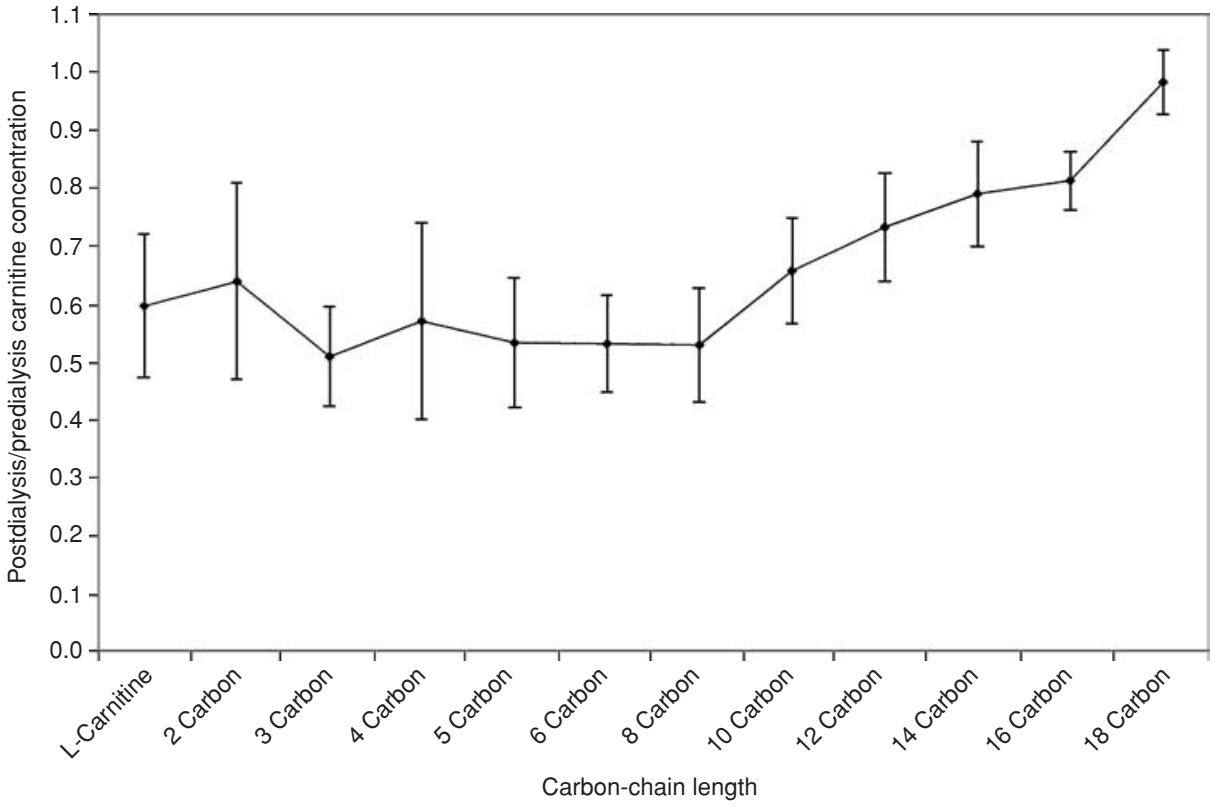

Fig. 1. Relationship between mean (± SEM) ratio of postdialysis/predialysis acylcarnitine concentrations and carbon-chain length of the acyl group.

significant correlation between carbon-chain length and dialytic removal (Fig. 1).

In light of these findings, we propose that, in combination with disturbed metabolism, the observed alterations in the carnitine pool are contributed to by a decrease in the dialytic removal of acylcarnitines, in particular long-chain acylcarnitines, most likely a result of the increased molecular weight and lipophilicity that accompanies increased chain length.

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Albuminuria in patients with hepatitis C: Is inflammation the missing link?

To the Editor: The study by Liangpunsakul and Chalasani on the association between hepatitis C and microalbuminuria reports an independent association between these 2 clinical entities [1]. The significance of their results may, however, be limited by the fact that their use of 1 albumin to creatinine ratio to measure microalbuminuria may be a source of error, including an underestimation of microalbuminuria in some some racial/ethnic groups [2].

Futhermore, their failure to find an association between hepatits C and the metabolic syndrome, may be explained by the fact that in at least in some age groups,